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HYPERTENSION OF RENAL VASCULAR ORIGIN*

The incidence of hypertensive vascular disease is estimated at 25 per cent in the population segment between the third and seventh decades of life.¹ Following Goldblatt's² experimental success in inducing hypertension in animals by partial occlusion of one or both renal arteries, clinical interest centered on possible reproduction of this entity in man. Early experience indicated that there were, indeed, parallels which could be drawn. Unfortunately, hypertensive patients were subjected to nephrectomy without much other indication than that hypertension was present and abnormality of one kidney suspected. The basic lesions in the renal vascular system causing hypertension were not only poorly understood, but techniques for studying and documenting them were inadequate. Predictably, results were unsatisfactory: Smith,¹ in 1956, reported that only 25 per cent of patients undergoing nephrectomy for unilateral renal disease associated with hypertension could meet his criteria for improvement. His report reflected the pessimism general among clinicians at that time.

Perhaps the most important single factor in improving this situation has been the refinement of angiographic methods for studying the renal arterial system. Renewed clinical study has resulted in the evolution of functional tests which are extremely helpful in establishing the indications for more extensive study, and, in some cases, for predicting the success of surgery. The preoperative delineation of the type, extent and unilateral or bilateral aspects of the vascular lesion has made it possible to plan the surgical attack. New developments in the rapidly expanding field of vascular surgery have resulted in improved techniques, particularly relating to vessel

repair, grafts and bypasses, making it possible to overcome clinical problems that hitherto would have been deemed inoperable.

The recent change in attitude towards this problem is illustrated in the contrasting nature of two reports only three years apart. Smith¹ stated that "of all patients with diastolic hypertension, probably less than two per cent are candidates for therapeutic renal surgery." In 1959, Poutasse³ reported that of 337 hypertensive patients seen during a four-year period, 87 (26 per cent) were found to have occlusive disease of one or both renal arteries and thus could be considered for surgical therapy.

The following considerations will indicate that history and physical examination contribute little to the recognition of renal artery disease as a cause of hypertension. There are certain adjunctive tests that suggest this diagnosis, but the clear and detailed picture is disclosed only by angiography.

History

There is no diagnostic history associated with the clinical syndrome of renal hypertension. We have been impressed with the small but significant number of patients who relate a history of trauma over the lumbar region in the remote or distant past. Dunn⁴ has been similarly impressed with this apparent relationship. A history of flank pain may be significantly related to embolization of the kidney.

Symptoms

There is no characteristic set of symptoms associated with hypertension due to renal abnormality. The symptoms are those protean ones characteristic of sustained hypertension, but usually include headache and visual disturbances.

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Physical examination is usually negative other than the finding of elevated blood pressure in both systolic and diastolic phases. However, auscultation over the upper abdomen may disclose the presence of a bruit with transmission to one or both costovertebral angles; this is suggestive of renal artery stenosis.

Etiology

The essential cause for the development of renal hypertension seems to be a change in renal hemodynamics in a part or all of one or both kidneys, secondary to stenosis in the arterial supply proximal to the renal parenchyma. Dustan, et al.,⁵ suggest that ischemia itself is not necessary, but that changes in the pulse pressure may be the essential factor in promoting the release of renin from the kidney. These authors state that renin has been found to be a proteolytic enzyme having the ability to split a polypeptide from a protein substrate synthesized by the liver. A converting enzyme in the blood splits histadyl-leucine from the decapeptide. The resulting octapeptide, called angiotensin, is a potent vasopressor agent. Pharmacologically, the effect of this agent is to increase peripheral resistance.

Pathological Anatomy

Poutasse³ reports that the majority of renal arterial occlusive lesions are arteriosclerotic plaques. The next most common lesion is fibromuscular subintimal proliferation, followed by thrombosis or aneurysm of the renal artery, or of one of its major branches. Occlusions involve either main arteries or branches of arteries and the infarctions correspond to the vessel involved. Trippel⁶ also lists thromboangiitis of the renal artery, coarctation of the abdominal aorta with renal stenosis, syphilitic arteritis, and narrowing of the artery due to pressure from extrinsic factors such as abdominal aortic aneurysm, extrinsic masses pressing on, and trauma to, the renal artery.

Which patient should undergo the detailed and expensive tests necessary to define accurately the presence of renal artery disease leading to hypertension? In view of the high incidence of hypertension cited above, it is obvious that there are neither facilities nor personnel available to test all the hypertensive population. Hypertension of sudden onset seems to be the most pressing indication for thorough study. Examination is also indicated in a hypertensive patient under 35 years of age or in the patient over 55 years of age in whom essential hypertension suddenly becomes malignant in character, in patients developing hypertension after an episode of flank or abdominal pain, or in patients whose intravenous urograms suggest certain abnormalities.⁵ However, it seems to us that a hypertensive patient at any age, whose

hypertension is shown not to be due to nephritis, pheochromocytoma, coarctation of the aorta, Cushing's syndrome, or primary hyperaldosteronism may well be a fit subject for study unless there are forbidding considerations relating to age and other infirmities.

Intravenous and Retrograde Pyelography

Excretory urography is a most important diagnostic tool in the examination of the hypertensive patient. We are particularly interested in evidences of disparity in size or in function between the two sides. Suggestive findings are: (1) differences in size of the two kidneys as measured on the x-ray film (differences in length of as little as 1 cm. are judged to be significant); and (2) delay in appearance of contrast material on one side as compared to the other has equal significance. The difference in appearance time may be noted in the five-minute film. There are usually no changes in the configuration of the pelvicalyceal system nor in the promptness of emptying between the two sides. However, intravenous urograms may appear entirely normal even in the presence of significant renal vascular disease.

The comparison of the relative functional capacities of the two kidneys is carried further by means of cystoscopy and retrograde catheterization of the ureters. The use of the Howard test may indicate important discrepancies between the two sides. Connor, et al.,⁷ suggested that a reduction of 50 per cent of the volume of fluid excreted and a reduction of 15 per cent in sodium excretion on the affected side as compared to the normal side were indications that the patient would benefit from operation on the affected kidney. Subsequently, Schlegel, and others,⁸ stated that "in the proven renal hypertensives, a definite pattern of higher urine osmolality, lower volume and usually higher potassium concentration and ammonia concentration, as well as lower pH, were found in the urine from the affected side." Nearly all observers have noted occasional departures from these concepts in patients in whom definite and remediable renal arterial lesions have been subsequently demonstrated.

It is apparent that if renal vessels on both sides are involved, there might not be any functional variation between the two kidneys. Moreover, segmental infarction might be of sufficient extent to cause hypertension, but still not influence excretion of water or solutes to the extent deemed significant.

A positive Howard test has important clinical meaning, but a negative test does not rule out the possibility of one or more renal vascular lesions being present.

Adjunctive Test for Differential Renal Function

A test for differential renal function was described by Winter,⁹ in 1956. A tracer dose of iodine I¹³¹ in the form of an organic iodide is injected intravenously and the amount of gamma ray activity over the kidneys is recorded by means of scintillometers placed simultaneously over each kidney area. A typical recording shows an initial vascular filling phase, a subsequent tubular concentration phase and a third upper urinary tract emptying phase. Impairment of the arterial supply to one kidney should result in a lowering of these values (particularly the first) as compared to the opposite side. This is almost entirely a qualitative and comparative test, but since it can be carried out on the ambulatory patient without any other manipulation than intravenous injection of the radioactive material, it may have important application in screening hypertensive patients to find those suitable for further study. Winter¹⁰ has more recently reported a 15 per cent false positive error in an extensive series of clinical tests. It is likely that this can be overcome by technical improvements in the method. The test is most appealing in its applicability to the mass screening of large segments of the hypertensive population.

Pharmacological Differentiation

Brust and Ferris¹¹ report that the rapid intravenous injection of 400 mg. of tetraethylammonium chloride (Etamon), causes a change in blood pressure characteristic of the modality responsible for hypertension. In cases of pheochromocytomas, there is an abrupt rise in blood pressure; in patients with renal artery disease, blood pressure remains level or shows a gradual rise. There is also a vasopressor response in acute nephritis, but usually this is clinically well differentiated from the hypertensive situations mentioned above. Patients with chronic nephritis or essential hypertension show a lowering of blood pressure in this test. However, there are few reports of the efficacy of this test, which has not been used extensively.

Aortography

All diagnostic tests mentioned above lead to aortography. Vascular disease of one kidney may be inferred from positive results of the Howard test, the radioactive Diodrast renogram and the intravenous pyelogram, but the extent and nature can only be ascertained by aortography. This is a procedure not without risk to kidneys, to mesenteric vessels and to spinal cord. However, Pou-tasse³ has carried out over 500 renal angiograms without mortality and only slight morbidity. He favors the translumbar intra-aortic injection.

In a smaller series, we have had no mortality and only one instance of unilateral renal shut-down following the use of translumbar aortography. Recently, however, we have been persuaded by C. T. Dotter¹² to employ the transfemoral artery catheterization technique with positioning of the arterial catheter under fluoroscopic control to allow accurate filling of the renal arteries with smaller volumes and strengths of contrast material. This has been one of three technical modifications in traditional aortographic techniques. The second improvement in technique has been the use of a pressure (Shipps') injector¹³ which insures a high volume of contrast material in the aorta and at the level of the renal arteries within a short period of time. The third advantageous step has been the use of the Sanchez Perez rapid cassette changer which allows a large number of films to be taken within a relatively short period of time and at the point of greatest filling of the renal arteries. These three modifications in technique have resulted in almost uniformly good renal angiograms and have made possible the visualization of renal artery lesions which were indefinable in our hands by translumbar aortography.

Management

Contrary to current belief, hypertension due to renal artery disease is often responsive to medical management. Thus Dustan, et al.,⁵ report that the blood pressure in such patients can be decreased by ganglion-blocking agents and reserpine. However, the decrease is usually not to normotensive levels and is generally not sustained.

Definitive response has been obtained through surgical intervention: by either nephrectomy on the affected side or removal of or bypassing the vascular lesion. In this connection, it is interesting to note that whereas earlier experience indicated that most good results were obtained by nephrectomy, more recently the emphasis has been upon removal of the vascular lesion and preservation of renal tissue. This is particularly in keeping with the recent concept that the kidney affected by the vascular lesion is also "protected" from the effects of hypertension, while the kidney on the opposite side, possessing a normal blood supply, is subjected to the full effects of the hypertension. Luke and Levitan¹⁴ have suggested that the affected kidney be "revascularized" by appropriate surgical techniques and that the opposite kidney then be removed. So far, however, there has been no evidence to indicate the degree to which the opposite kidney may recover after hypertensive levels have been alleviated. It is also possible that where hypertension remains "fixed" after surgery, there still remains an undiscovered renal vascular lesion.

The alternative surgical procedures which have been described for restoration of normal blood flow through one or both kidneys have been enumerated by Trippel. Of the numerous techniques illustrated, the particular one chosen will depend upon the clinical situation existing and the training and preferences of the surgeon.

Results

In the largest series, that of Poutasse, about 80 per cent of hypertensive patients with occlusive disease of renal arteries who have survived surgical treatment have been benefited by either attaining normal blood pressure or a residual systolic hypertension with normal diastolic pressure. Almost all other series are too small to permit careful evaluation, but the clinical impression is that the results of corrective surgery are usually either good or nil.

In our patients, the blood pressure usually has fallen gradually over a period of 8 to 10 hours following surgery and has sometimes then required support with vasopressors for two to three days before leveling out in normotensive ranges. However, Brust and Ferris¹¹ have described normotensive responses delayed up to 10 and 12 days postoperatively, and have also noted mild labile hypertension up to six months postoperatively before normotension was restored.

Conclusions

At the present time, certain general observations may be made. The incidence of hypertension due to renal artery occlusive disease is much higher than previously disclosed. The presence of renal artery lesions can be suspected through the use of several indirect tests. These tests may indicate those patients who should be subjected to angiography. Unilateral or bilateral renal artery lesions can be diagnosed precisely by

means of angiography. Surgical techniques, still in the formative and exploratory stage, give promise of affording relief to a high percentage of patients afflicted.

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